

CG37957-391795

CGGGGGAAGAAGATGTGAAGTCTTTTCCCTCCG 33

CAGAAGAAGAGCCCTTTTTTTCCTCCGCGAAGGCCAATGTTCTCAAAAAGCTCTAG 93

ATGGGAATGGCTGCTTACATGACAGAAATCGAGGCAAGCTCCATCTCTCTGTACAT 153
R G N A C L T H T E N E A T S T S F V H 20

CAGAATGGTGATATTCCTGGAAGTCTAATCTCTGAAGCAGATAGAGCAGCTCTCAA 213
Q M G D I P G E A N S V K Q I E P V L Q 40

GTGTATCTGTACCATCTCTCTGGGCAAGCTGAAGCAGATATCTGAAGTTCCAAAGTGA 273
V Y L Y N S L G Q A E C E Y L K F P S G 60

CAGTATGTTGCAGAGAATTTTCTGTGGCTGCTTCTAAAGCTTGTGATTACGGCTGTG 333
E Y V A E E E C V A A S K A C G I T F V 80

TATCATAATATCTTTGCTTAACTAGTGAAGCCGAAGGCTGTGACCCACCAATCAT 393
Y K N H F A L N S E T E R I M Y F P N H 100

GTCTTCACATAGACAGTCAACGAGGATGACATACCTTACAGGATAAGGTTCTACTTC 453
V F H I D E S T R H D I L Y R I R F Y F 120

CCTCATTTGCTACTGTAGTGGCAGCAGCAGAACTACAGATACGAGTGTCCGCTGGGGCT 513
P H M Y C S G S E R T Y G V S R G A 140

GAAGCTCTCTCTCTGAGTACTTGTGATGCTTACTTTTGGTGGAGTGGGGCATGAT 573
E A F L L D D F V N S Y L F A Q W R N D 160

TTTGTTCAGGATGATATAAAGTACCTGTGACTCATGAAGCTCAGCAAGAGCTGTCTGG 633
F V H G M I K V P V T R E T Q E E C L G 180

ATGGGGCTTTAGACATGATGAGAATAGCTAAGCAGAAAGCAGAGCTCCACTGGCTGTG 693
M A V L D N H R I A K E K D Q T F L A V 200

TATAACTCTGTGAGTACAGACATCTTACCAAGTGGCTTGGAGGAGATGCAAGAC 753
Y N S V S Y K T F L F K C V R A K I Q D 220

TATCAGATTTTAAAGGAGCAAGCAAGTACAGATTTGGAGATTCAGCAATTC 813
Y H I L T R K R I R Y R F R F I Q Q F 240

AGTCAATGTAAAGCAGCTCCAGCAAGCTTAAAGTCTTATATCTTATAAGCTGCAAGC 873
S Q C H K S A W T A W R N H L K E T L D I L E T 260

CTGCAGTGTGGCTTACACAGAACAGTTTGAAGTAAAGAACTCTCAAGAGCTGCTTCA 933
L Q S A F Y T E Q F E V K E S A R G F S 280

CGTGAGGAGATTTTGCAGCAATTATAAAGTGAAGGCTGGAATTCAGTGTGCAAGA 993
G E E I F A T I I I T G N G G I Q W S R 300

CGGAACATAAGGAAGTGCACACTGCAGCAAGCAGCAAGCTACAGTATATGTGATTC 1053
G K H K E S E T L T E Q D V Q L Y C D F 320

CCTGATATTATTCATCTCAGTATTAGCAAGCAAGCAAGCAAGCTGCAAGTACA 1113
P D I I D V S I K Q A N Q E C S K E S R 340

ATTCTAAGTGTGATTAAGCAAGCAAGCAAGCAAGCTGCAAGTACAAGTACA 1173
I V T V H K Q D C K V L E I E L S L K 360

- FIGURE 1A -

53397357-091709

GAAGCCTTCTCATTCTGTCATTAAATTCAGCGGTATTACAGACTAACTGGCGATGGCAC 1233
 KALEFVSELDIGYYRLTADAH 360

CATTACCTTCGAAGAGCGTGGCTGGCGAGTCTGCTGCGAGAAATACACAGCAACTGC 1293
 HYLCKEVAFFPAVLENIHMKC 400

CAGCGGCGCAATATCAATGCTTTTGGCATTAGCAAACTAAAGAGCGCGGCTAAACAGACT 1353
 HCFLEKDFATISKLEKAKNQ 420

CGCATATATGCTGCTAGATGCGAGCGCTAAGGAGCTTCAACAAATAGTTTCTCACCTTTGCT 1413
 CLYVLRKCEPKDFKKYFLTF 440

GTTGAGCGAGAAATGTCATTGATATAAAGACTGTTTTCATTACGAAGATCAGAATCGA 1473
 VERENXVIEYKHCLETKENG 460

GAATACAACTCAGCGGAGCTAAGAGGAGCTTCAAGCTTAAAGACCTTTTGAATTC 1533
 EYKLESGCTKRNFESLKDLLNC 480

TACGAGATCGAACTGTGGCGTCAGACGATATCATCTTTCAGCTTACCAAAATGCTGGCG 1593
 YQKETVREDESLFQFTTKCCP 500

CGAAGCGAAGGATAAATCAAACTTCTGCTTTCAGACAAATGCTATTCTCATCTT 1653
 FKFPRDKSKLLVFRTKGCSOV 520

CGCATCTCAGCAAGATTACAGAGCGCTAATAATGCTGAATCAATGCTTTCAGAAATC 1713
 QIESFTLQRRHKKVKNQNVFRK 540

AGCAATGAGATTATATTTAATGAAGCTTTCGCGAGCTTTTACAAAAATTTT 1773
 RKEIDLIFKCSLGCCTFTTKIF 560

AAAGGTGAAGAGAGTTCGAGATTATGCTGCTGAGCAAAAGCGAGCTTTTTC 1833
 KGVRRREVGDYCGQLHKTEVLL 580

AAAGTCTAGATAAGACATAGCACTATTGAGAGCTTTTTCGAAAGCAAGCATC 1893
 KYLDKAKRXYSESEFFFAASK 600

ATGAGTCAGCTTCTCAGAGCATTTGCTTGAATATGCTGCTGCTGCTGCTGAGAG 1953
 KSQLSEHKNLVLYNYGVCVCGE 620

GAGAGCTTCTGCTCAGAGATTGTAAATTTGGTCACTGATACCTAAGTGAAGAG 2013
 ENILVQGFVKFGSLDTYLLK 640

AGCAAAATGCAATAATATATATGCAAACTTGGAGTGGCTAAGCAGTTGGCATGGGCG 2073
 KKSINILWKLGVAKQLAWA 660

ATGCAATTTCTGAGAGAAAAATGCTTATTATGCGAATGCTGCTGCTAAGAAATATCTCT 2133
 KHFLEEKESLINGVCAKNIL 680

CTTATCAG 2193
 LIREEDRRTGRTFFFIKLSDF 700

GCGATTAGCATTACAGTTGTACAGAGGAGCTTCTTCAGAGAGAGAGAGAGAGAGAGAGAG 2253
 GISTITVLPKDI-LQERIFWVF 720

CCTGAATGCTGAGAGATGCTAAGAAATCTCAATCTGCGCAAGAGAGAGAGAGAGAGAGAG 2313
 FCEIENPKNLNLATDKWSEFG 740

AACACTCTGCGAGAGATGCGAGTGGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAGAG 2373
 TLTWEICSGGDKPLSALDESQ 760

- FIGURE 1B -

0337567-031799

ACAAAGCTGCAGTTCTATCAAGATAAGCATCAGCTTCTGTCACCCAGTGCACAGAGTTA⁹ 2433
 R K E L Q F Y E D K H Q L P A F R M T E L 780
 GCAAAAGCTTATAATAATTCATGCGACTATCAGCCAGATTTCAGCCGCTTCCTTCAGAGCT 2493
 A K L E M K C N D Y E P D F R P A F R A 800
 GTATCGCTGATCTTAAACAGCGCTGTTTACTCCAGATTATCAACTAGTAAACAGAAATGAC 2553
 V I R D L K S L F T P D Y E L L T E K D 820
 ATGCTACCAACATGCAATAGGTGCGCTTACGGGTTTCTGCTGCTTTTGAAGCAGCGGAC 2613
 H L P K M R I G A L C F S G A F E D R D 840
 CCTACACAGTTTGAAGAGAGACACITGAAGTTTCTACAGCAGCTTCGCAAGGTAACITC 2673
 P T Q F E E R H L K F L Q Q L G K K N F 860
 GGGAGTGTGAGATGTCCCGCTATGACCGCGCTGAGGACAACTGGGAGCTGGTGGCT 2733
 G E V E H C R Y D P L Q D N T G E V V A 880
 GTGAAGAACTGCAGCAGCAGCTCAAGAGCACTTCGAGAGCTTCAGAGCGGAGATGAG 2793
 V K K L Q H E T E E H L R D F E R E E 900
 ATCTGAATCTGTCAGCATGACAACTGCTCAAGTACAGGAGGATGTGCTACAGTGG 2853
 I L K S L Q H D N I V K Y K G V C Y E A 920
 GGTGGGCGCACTAAGATTATATTCGAATATTTAOCATATGGAGTTTACGAGAGTAT 2913
 G R R N L R L I K E Y L F I G S L R D Y 940
 CTCGAAAAACATAAAGAGGATAGATCAGAAAAACTCTCTCAATACACATCTCAGATA 2973
 L Q K K K E R I D H K K L L Q Y T S Q I 960
 TGCAGGGCGCATGGAATATCTTGTACAAAAAGGTATATCCACAGGCACTTCGCAAGAG 3033
 C K G K E Y L G T K R Y I H R D L A T R 980
 AACATATCTGTGAAAAATGAGAACAGGCTTAAATAGGAGAGCTTCGATTAAACAAAGTC 3093
 N I L V E K E N R V K I G D F C L T K V 1000
 TTGCGGCGAGCAAGAACTACTACAAAGTAAAGAGCGAGCGGCAAGCGCCATATCTGG 3153
 L P Q D K E Y Y K V K E F G E S F I F W 1020
 TAAGCACTGAATCTTGAAGGAGAGCAAGTTTCTGCTGCTGCTGAGATCTGTGGAGCTT 3213
 I A P E E L T E K F E V A S D V W S F 1040
 GAGTGTGCTTATACGAAGCTTTTACATACATGAGAGAGTAAAGTCCAGCGCTGGA 3273
 G V V L Y E L F T Y I E K S K S F F V E 1060
 TTTATCGGAATGATTGGCAATGATAAACAAGGCAATGATGTGTTCATTGTATAGAG 3333
 F R K N I G N D K Q G Q K I V F H L I E 1080
 CTACTGAAGAGCAAGGGAAGATTGCGAAGGCGAGAGGATGCCAGATGAGATTATGTG 3393
 L L K E N G R L P R F E G C F D E I Y V 1100
 ATCATGACAGAGCTGCTGCAACACAAATGTGAGCGAGGCTGCTGCTTCAGGAGCGTTTC^C 3453
 I N T E C W K N N V S Q R P S F R D L S 1120
 TTGCGGTGATCAAAATCGGACAGTATAGCTGCTGCTGGAAGAGATGCGCTTCACTCAGAG 3513
 F C W I K S G T V > 1129
 ACCAAGCAGAGTTCAGAAACAGAAAGCTGCTGAGCTGTGTCTACACATCTTAT 3573
 C (a) (a)
 CATGATGCTAGCTAGGCGAGAAAGCTGTAAGCGGCTGCTGCTCAAGCTTTGCTTC 3629
 C (a)

Human JAK1

ATG GCT TTC TGT GCT AAA ATG AGG AGC TCC AAG AAG ACT GAG GTG AAC Met Ala Phe Cys Ala Lys Met Arg Ser Ser Lys Lys Thr Glu Val Asn	123 16
CTG GAG GCC CCT GAG CCA GGG GTG GAA GTG ATC TTC TAT CTG TCG GAC Leu Glu Ala Pro Glu Pro Gly Val Glu Val Ile Phe Tyr Leu Ser Asp	171 32
AGG GAG CCC CTC CGG CTG GGC AGT GGA GAG TAC ACA GCA GAG GAA CTG Arg Glu Pro Leu Arg Leu Gly Ser Gly Glu Tyr Thr Ala Glu Glu Leu	219 48
TGC ATC AGG GCT GCA CAG GCA TGC CGT ATC TCT CCT CTT TGT CAC AAC Cys Ile Arg Ala Ala Gln Ala Cys Arg Ile Ser Pro Leu Cys His Asn	267 64
CTC TTT GCC CTG TAT GAC GAG AAC ACC AAG CTC TGG TAT GCT CCA AAT Leu Phe Ala Leu Tyr Asp Glu Asn Thr Lys Leu Trp Tyr Ala Pro Asn	315 80
CGC ACC ATC ACC GTT GAT GAC AAG ATG TCC CTC CGG CTC CAC TAC CGG Arg Thr Ile Thr Val Asp Asp Lys Met Ser Leu Arg Leu His Tyr Arg	363 96
ATG AGG TTC TAT TTC ACC AAT TGG CAT GGA ACC AAC GAC AAT GAG CAG Met Arg Phe Tyr Phe Thr Asn Trp His Gly Thr Asn Asp Asn Glu Gln	411 112
TCA GTG TGG CGT CAT TCT CCA AAG AAG CAG AAA AAT GGC TAC GAG AAA Ser Val Trp Arg His Ser Pro Lys Lys Gln Lys Asn Gly Tyr Glu Lys	459 128
AAA AAG ATT CCA GAT GCA ACC CCT CTC CTT GAT GCC AGC TCA CTG GAG Lys Lys Ile Pro Asp Ala Thr Pro Leu Leu Asp Ala Ser Ser Lys Glu	507 144
TAT CTG TTT GCT CAG GGA CAG TAT GAT TTG GTG AAA TGC CTG GCT CCT Tyr Leu Phe Ala Gln Gly Gln Tyr Asp Leu Val Lys Cys Leu Ala Pro	555 160
ATT CGA GAC CCC AAG ACC GAG CAG GAT GGA CAT GAT ATT GAG AAC GAG Ile Arg Asp Pro Lys Thr Glu Gln Asp Gly His Asp Ile Glu Asn Glu	603 176
TGT CTA GGG ATG GCT GTC CTG GCC ATC TCA CAC TAT GCC ATG ATG AAG Cys Leu Gly Met Ala Val Leu Ala Ile Ser His Tyr Ala Met Met Lys	651 192
AAG ATG CAG TTG CCA GAA CTG CCC AAG GAC ATC AGC TAC AAG CGA TAT Lys Met Gln Leu Pro Glu Leu Pro Lys Asp Ile Ser Tyr Lys Arg Tyr	699 208
ATT CCA GAA ACA TTG AAT AAG TCC ATC AGA CAG AGG AAC CTT CTC ACC Ile Pro Glu Thr Leu Asn Lys Ser Ile Arg Gln Arg Asn Leu Leu Thr	747 224
AGG ATG CGG ATA AAT AAT GTT TTC AAG GAT TTC CTA AAG GAA TTT AAC Arg Met Arg Ile Asn Asn Val Phe Lys Asp Phe Leu Lys Glu Phe Asn	795 240
AAC AAG ACC ATT TGT GAC AGC AGC GTG TCC ACG CAT GAC CTG AAG GTG Asn Lys Thr Ile Cys Asp Ser Ser Val Ser Thr His Asp Leu Lys Val	843 256
AAA TAC TTG GCT ACC TTG GAA ACT TTG ACA AAA CAT TAC GGT GCT GAA Lys Tyr Leu Ala Thr Leu Glu Thr Leu Thr Lys His Tyr Gly Ala Glu	891 272

FIGURE 2 A-

ATA TTT GAG ACT TCC ATG TTA CTG ATT TCA TCA GAA AAT GAG ATG AAT Ile Phe Glu Thr Ser Met Leu Leu Ile Ser Ser Glu Asn Glu Met Asn	939 288
TGG TTT CAT TCG AAT GAC GGT GGA AAC GTT CTC TAC TAC GAA GTG ATG Trp Phe His Ser Asn Asp Gly Gly Asn Val Leu Tyr Tyr Glu Val Met	987 304
GTG ACT GGG AAT CTT GGA ATC CAG TGG AGG CAT AAA CCA AAT GTT GTT Val Thr Gly Asn Leu Gly Ile Gln Trp Arg His Lys Pro Asn Val Val	1035 320
TCT GTT GAA AAG GAA AAA AAT AAA CTG AAG CGG AAA AAA CTG GAA AAT Ser Val Glu Lys Glu Lys Asn Lys Leu Lys Arg Lys Lys Leu Glu Asn	1083 336
AAA GAC AAG AAG GAT GAG GAG AAA AAC AAG ATC CGG GAA GAG TGG AAC Lys Asp Lys Lys Asp Glu Glu Lys Asn Lys Ile Arg Glu Glu Trp Asn	1131 352
AAT TTT TCA TTC TTC CCT GAA ATC ACT CAC ATT GTA ATA AAG GAG TCT Asn Phe Ser Phe Phe Pro Glu Ile Thr His Ile Val Ile Lys Glu Ser	1179 368
GTG GTC AGC ATT AAC AAG CAG GAC AAC AAG AAA ATG GAA CTG AAG CTC Val Val Ser Ile Asn Lys Gln Asp Asn Lys Lys Met Glu Leu Lys Leu	1227 384
TCT TCC CAC GAG GAG GCC TTG TCC TTT GTG TCC CTG GTA GAT GGC TAC Ser Ser His Glu Glu Ala Leu Ser Phe Val Ser Leu Val Asp Gly Tyr	1275 400
TTC CGG CTC ACA GCA GAT GCC CAT CAT TAC CTC TGC ACC GAC GTG GCC Phe Arg Leu Thr Ala Asp Ala His His Tyr Leu Cys Thr Asp Val Ala	1323 416
CCC CGG TTG ATC GTC CAC AAC ATA CAG AAT GGC TGT CAT GGT CCA ATC Pro Pro Leu Ile Val His Asn Ile Gln Asn Gly Cys His Gly Pro Ile	1371 432
TGT ACA GAA TAC GCC ATC AAT AAA TTG CGG CAA GAA GGA AGC GAG GAG Cys Thr Glu Tyr Ala Ile Asn Lys Leu Arg Gln Glu Gly Ser Glu Glu	1419 448
GGG ATG TAC GTG CTG AGG TGG AGC TGC ACC GAC TTT GAC AAC ATC CTC Gly Met Tyr Val Leu Arg Trp Ser Cys Thr Asp Phe Asp Asn Ile Leu	1467 464
ATG ACC GTC ACC TGC TTT GAG AAG TCT GAG CAG GTG CAG GGT GCC CAG Met Thr Val Thr Cys Phe Glu Lys Ser Glu Gln Val Gln Gly Ala Gln	1515 480
AAG CAG TTC AAG AAC TTT CAG ATC GAG GTG CAG AAG GGC CGC TAC AGT Lys Gln Phe Lys Asn Phe Gln Ile Glu Val Gln Lys Gly Arg Tyr Ser	1563 496
CTG CAC GGT TCG GAC CGC AGC TTC CCC AGC TTG GGA GAC CTC ATG AGC Leu His Gly Ser Asp Arg Ser Phe Pro Ser Leu Gly Asp Leu Met Ser	1611 512
CAC CTC AAG AAG CAG ATC CTG CGC ACG GAT AAC ATC AGC TTC ATG CTA His Leu Lys Lys Gln Ile Leu Arg Thr Asp Asn Ile Ser Phe Met Leu	1659 528
AAA CGC TGC TGC CAG CCC AAG CCC CGA GAA ATC TCC AAC CTG CTG GTG Lys Arg Cys Cys Gln Pro Lys Pro Arg Glu Ile Ser Asn Leu Leu Val	1707 544
GCT ACT AAG AAA GCC CAG GAG TGG CAG CCC GTC TAC CCC ATG AGC CAG Ala Thr Lys Lys Ala Gln Glu Trp Gln Pro Val Tyr Pro Met Ser Gln	1755 560

- FIGURE 2 B -

0337357-031703

CTG AGT TTC GAT CGG ATC CTC AAG AAG GAT CTG GTG CAG GGC GAG CAC Leu Ser Phe Asp Arg Ile Leu Lys Lys Asp Leu Val Gln Gly Glu His	1803 576
CTT GGG AGA GGC ACG AGA ACA CAC ATC TAT TCT GGG ACC CTG ATG GAT Leu Gly Arg Gly Thr Arg Thr His Ile Tyr Ser Gly Thr Leu Met Asp	1851 592
TAC AAG GAT GAC GAA GGA ACT TCT GAA GAG AAG AAG ATA AAA GTG ATC Tyr Lys Asp Asp Glu Gly Thr Ser Glu Glu Lys Lys Ile Lys Val Ile	1899 608
CTC AAA GTC TTA GAC CCC AGC CAC AGG GAT ATT TCC CTG GCC TTC TTC Leu Lys Val Leu Asp Pro Ser His Arg Asp Ile Ser Leu Ala Phe Phe	1947 624
GAG GCA GCC AGC ATG ATG AGA CAG GTC TCC CAC AAA CAC ATC GTG TAC Glu Ala Ala Ser Met Met Arg Gln Val Ser His Lys His Ile Val Tyr	1995 640
CTC TAT GGC GTC TGT GTC CGC GAC GTG GAG AAT ATC ATG GTG GAA GAG Leu Tyr Gly Val Cys Val Arg Asp Val Glu Asn Ile Met Val Glu Glu	2043 656
TTT GTG GAA GGG GGT CCT CTG GAT CTC TTC ATG CAC CGG AAA AGT GAT Phe Val Glu Gly Gly Pro Leu Asp Leu Phe Met His Arg Lys Ser Asp	2091 672
GTC CTT ACC ACA CCA TGG AAA TTC AAA GTT GCC AAA CAG CTG GCC AGT Val Leu Thr Thr Pro Trp Lys Phe Lys Val Ala Lys Gln Leu Ala Ser	2139 688
GCC CTG AGC TAC TTG GAG GAT AAA GAC CTG GTC CAT GGA AAT GTG TGT Ala Leu Ser Tyr Leu Glu Asp Lys Asp Leu Val His Gly Asn Val Cys	2187 704
ACT AAA AAC CTC CTC CTG GCC CGT GAG GGA ATC GAC AGT GAG TGT GGC Thr Lys Asn Leu Leu Ala Arg Glu Gly Ile Asp Ser Glu Cys Gly	2235 720
CCA TTC ATC AAG CTC AGT GAC CCC GGC ATC CCC ATT ACG GTG CTG TCT Pro Phe Ile Lys Leu Ser Asp Pro Gly Ile Pro Ile Thr Val Leu Ser	2283 736
AGG CAA GAA TGC ATT GAA CGA ATC CCA TGG ATT GCT CCT GAG TGT GTT Arg Gln Glu Cys Ile Glu Arg Ile Pro Trp Ile Ala Pro Glu Cys Val	2331 752
GAG GAC TCC AAG AAC CTG AGT GTG GCT GCT GAC AAG TGG AGC TTT GGA Glu Asp Ser Lys Asn Leu Ser Val Ala Ala Asp Lys Trp Ser Phe Gly	2379 768
ACC ACG CTC TGG GAA ATC TGC TAC AAT GGC GAG ATC CCC TTG AAA GAC Thr Thr Leu Trp Glu Ile Cys Tyr Asn Gly Glu Ile Pro Leu Lys Asp	2427 784
AAG ACG CTG ATT GAG AAA GAG AGA TTC TAT GAA AGC CGG TGC AGG CCA Lys Thr Leu Ile Glu Lys Glu Arg Phe Tyr Glu Ser Arg Cys Arg Pro	2475 800
GTG ACA CCA TCA TGT AAG GAG CTG GCT GAC CTC ATG ACC CGC TGC ATG Val Thr Pro Ser Cys Lys Glu Leu Ala Asp Leu Met Thr Arg Cys Met	2523 816
AAC TAT GAC CCC AAT CAG AGG CCT TTC TTC CGA GCC ATC ATG AGA GAC Asn Tyr Asp Pro Asn Gln Arg Pro Phe Phe Arg Ala Ile Met Arg Asp	2571 832
ATT AAT AAG CTT GAA GAG CAG AAT CCA GAT ATT GTT TCC AGA AAA AAA Ile Asn Lys Leu Glu Glu Gln Asn Pro Asp Ile Val Ser Arg Lys Lys	2619 848

- FIGURE 2c -

AAC CAG CCA ACT GAA GTG GAC CCC ACA CAT TTT GAG AAG CGC TTC CTA Asn Gln Pro Thr Glu Val Asp Pro Thr His Phe Glu Lys Arg Phe Leu	2667 864
AAG AGG ATC CGT GAC TTG GGA GAG GGC CAC TTT GGG AAG GTT GAG CTC Lys Arg Ile Arg Asp Leu Gly Glu Gly His Phe Gly Lys Val Glu Leu	2715 880
TGC AGG TAT GAC CCC GAA GAC AAT ACA GGG GAG CAG GTG GCT GTT AAA Cys Arg Tyr Asp Pro Glu Asp Asn Thr Gly Glu Gln Val Ala Val Lys	2763 896
TCT CTG AAG CCT GAG AGT GGA GGT AAC CAC ATA GCT GAT CTG AAA AAG Ser Leu Lys Pro Glu Ser Gly Gly Asn His Ile Ala Asp Leu Lys Lys	2811 912
GAA ATC GAG ATC TTA AGG AAC CTC TAT CAT GAG AAC ATT GTG AAG TAC Glu Ile Glu Ile Leu Arg Asn Leu Tyr His Glu Asn Ile Val Lys Tyr	2859 928
AAA GGA ATC TGC ACA GAA GAC GGA GGA AAT GGT ATT AAG CTC ATC ATG Lys Gly Ile Cys Thr Glu Asp Gly Gly Asn Gly Ile Lys Leu Ile Met	2907 944
GAA TTT CTG CCT TCG GGA AGC CTT AAG GAA TAT CTT CCA AAG AAT AAG Glu Phe Leu Pro Ser Gly Ser Leu Lys Glu Tyr Leu Pro Lys Asn Lys	2955 960
AAC AAA ATA AAC CTC AAA CAG CAG CTA AAA TAT GCC GTT CAG ATT TGT Asn Lys Ile Asn Leu Lys Gln Gln Leu Lys Tyr Ala Val Gln Ile Cys	3003 976
AAG GGG ATG GAC TAT TTG GGT TCT CGG CAA TAC GTT CAC CGG GAC TTG Lys Gly Met Asp Tyr Leu Gly Ser Arg Gln Tyr Val His Asp Ser Leu	3051 992
GCA GCA AGA AAT GTC CTT GTT GAG AGT GAA CAC CAA GTG AAA ATT GGA Ala Ala Arg Asn Val Leu Val Glu Ser Glu His Gln Val Lys Ile Gly	3099 1008
GAC TTC GGT TTA ACC AAA GCA ATT GAA ACC GAT AAG GAG TAT TAC ACC Asp Phe Gly Leu Thr Lys Ala Ile Glu Thr Asp Lys Glu Tyr Tyr Thr	3147 1024
GTC AAG GAT GAC CGG GAC AGC CCT GTG TTT TGG TAT GCT CCA GAA TGT Val Lys Asp Asp Arg Asp Ser Pro Val Phe Trp Tyr Ala Pro Glu Cys	3195 1040
TTA ATG CAA TCT AAA TTT TAT ATT GCC TCT GAC GTC TGG TCT TTT GGA Leu Met Gln Ser Lys Phe Tyr Ile Ala Ser Asp Val Trp Ser Phe Gly	3243 1056
GTC ACT CTG CAT GAG CTG CTG ACT TAC TGT GAT TCA GAT TCT AGT CCC Val Thr Leu His Glu Leu Leu Thr Tyr Cys Asp Ser Asp Ser Ser Pro	3291 1072
ATG GCT TTG TTC CTG AAA ATG ATA GGC CCA ACC CAT GGC CAG ATG ACA Met Ala Leu Phe Leu Lys Met Ile Gly Pro Thr His Gly Gln Met Thr	3339 1088
GTC ACA AGA CTT GTG AAT ACG TTA AAA GAA GGA AAA CGC CTG CGG TGC Val Thr Arg Leu Val Asn Thr Leu Lys Glu Gly Lys Arg Leu Pro Cys	3387 1104
CCA CCT AAC TGT CCA GAT GAG GTT TAT CAG CTT ATG AGA AAA TGC TGG Pro Pro Asn Cys Pro Asp Glu Val Tyr Gln Leu Met Arg Lys Cys Trp	3435 1120
GAA TTC CAA CCA TCC AAT CGG ACA AGC TTT CAG AAC CTT ATT GAA GGA Glu Phe Gln Pro Ser Asn Arg Thr Ser Phe Gln Asn Leu Ile Glu Gly	3483 1136

- FIGURE 2 D -

TTT GAA GCA CTT TTA AAA TAA
Phe Glu Ala Leu Leu Lys

3504
1143

00337557 001790
002760 1507650

Human TYK2

ATG CCT CTG CGC CAC TGG GGG ATG GCC AGG GGC AGT AAG CCC GTT GGG Met Pro Leu Arg His Trp Gly Met Ala Arg Gly Ser Lys Pro Val Gly	354 16
GAT GGA GCC CAG CCC ATG GCT GCC ATG GGA GGC CTG AAG GTG CTT CTG Asp Gly Ala Gln Pro Met Ala Ala Met Gly Gly Leu Lys Val Leu Leu	402 32
CAC TGG GCT GGT CCA GGC GGC GGG GAG CCC TGG GTC ACT TTC AGT GAG His Trp Ala Gly Pro Gly Gly Gly Glu Pro Trp Val Thr Phe Ser Glu	450 48
TCA TCG CTG ACA GCT GAG GAA GTC TGC ATC CAC ATT GCA CAT AAA GTT Ser Ser Leu Thr Ala Glu Glu Val Cys Ile His Ile Ala His Lys Val	498 64
GGT ATC ACT CCT CCT TGC TTC AAT CTC TTT GCC CTC TTC GAT GCT CAG Gly Ile Thr Pro Pro Cys Phe Asn Leu Phe Ala Leu Phe Asp Ala Gln	546 80
GCC CAA GTC TGG TTG CCC CCA AAC CAC ATC CTA GAG ATC CCC AGA GAT Ala Gln Val Trp Leu Pro Pro Asn His Ile Leu Glu Ile Pro Arg Asp	594 96
GCA AGC CTG ATG CTA TAT TTC CGC ATA AGG TTT TAT TTC CGG AAC TGG Ala Ser Leu Met Leu Tyr Phe Arg Ile Arg Phe Tyr Phe Arg Asn Trp	642 112
CAT GGC ATG AAT CCT CGG GAA CCG GCT GTG TAC CGT TGT GGG CCC CCA His Gly Met Asn Pro Arg Glu Pro Ala Val Tyr Arg Cys Gly Pro Pro	690 128
GGA ACC GAG GCA TCC TCA GAT CAG ACA GCA CAG GGG ATG CAA CTC CTG Gly Thr Glu Ala Ser Ser Asp Gln Thr Ala Gln Gly Met Gln Leu Leu	738 144
GAC CCA GCC TCA TTT GAG TAC CTC TTT GAG CAG GGC AAG CAT GAG TTT Asp Pro Ala Ser Phe Glu Tyr Leu Phe Glu Gln Gly Lys His Glu Phe	786 160
GTG AAT GAC GTG GCA TCA CTG TGG GAG CTG TCG ACC GAG GAG GAG ATC Val Asn Asp Val Ala Ser Leu Trp Glu Leu Ser Thr Glu Glu Glu Ile	834 176
CAC CAC TTT AAG AAT GAG AGC CTG GGC ATG GCC TTT CTG CAC CTC TGT His His Phe Lys Asn Glu Ser Leu Gly Met Ala Phe Leu His Leu Cys	882 192
CAC CTC GCT CTC CGC CAT GGC ATC CCC CTG GAG GAG GTG GCC AAG AAG His Leu Ala Leu Arg His Gly Ile Pro Leu Glu Glu Val Ala Lys Lys	930 208
ACC AGC TTC AAG GAC TGC ATC CCG CGC TCC TTC CGC CGG CAT ATC CGG Thr Ser Phe Lys Asp Cys Ile Pro Arg Ser Phe Arg Arg His Ile Arg	978 224
CAG CAC AGC GCC CTG ACC CGG CTG CGC CIT CGG AAC GTC TTC CGC AGG Gln His Ser Ala Leu Thr Arg Leu Arg Leu Arg Asn Val Phe Arg Arg	1026 240
TTT CTG CGG GAC TTC CAG CCG GGC CGA CTC TCC CAG CAG ATG GTC ATG Phe Leu Arg Asp Phe Gln Pro Gly Arg Leu Ser Gln Gln Met Val Met	1074 256
GTC AAA TAC CTA GCC ACA CTC GAG CCG CTG GCA CCC CGC TTC GGC ACA Val Lys Tyr Leu Ala Thr Leu Glu Arg Leu Ala Pro Arg Phe Gly Thr	1122 272

- FIGURE 3 A-

CTC ATC ATC ATG CCG GGG GCT CCG GCC AGC CCC AGG ACA CTC AAC CTC	2034
Leu Ile Ile Met Arg Gly Ala Arg Ala Ser Pro Arg Thr Leu Asn Leu	576
AGC CAG CTC AGC TTC CAC CCG GTT GAC CAG AAG GAG ATC ACC CAG CTG	2082
Ser Gln Leu Ser Phe His Arg Val Asp Gln Lys Glu Ile Thr Gln Leu	592
TCC CAC TTG GGC CAG CGC ACA AGG ACC AAC GTG TAT GAG GGC CGC CTG	2130
Ser His Leu Gly Gln Gly Thr Arg Thr Asn Val Tyr Glu Gly Arg Leu	608
CGA GTG GAG GGC AGC GGG GAC CCT GAG GAG GGC AAG ATG GAT GAC GAG	2178
Arg Val Glu Gly-Ser Gly Asp Pro Glu Glu Gly Lys Met Asp Asp Glu	624
GAC CCC CTC GTG CCT GGC AGG GAC CGT GGG CAG GAG CTA CGA GTG GTG	2226
Asp Pro Leu Val Pro Gly Arg Asp Arg Gly Gln Glu Leu Arg Val Val	640
CTC AAA GTG CTG GAC CCT AGT CAC CAT GAC ATC GCC CTG GCC TTC TAC	2274
Leu Lys Val Leu Asp Pro Ser His His Asp Ile Ala Leu Ala Phe Tyr	656
GAG ACA GCC AGC CTC ATG AGC CAG GTC TCC CAC ACG CAC CTG GCC TTC	2322
Glu Thr Ala Ser Leu Met Ser Gln Val Ser His Thr His Leu Ala Phe	672
GTG CAT GGC GTC TGT GTG CGC GGC CCT GAA AAT AGC ATG GTG ACA GAG	2370
Val His Gly Val Cys Val Arg Gly Pro Glu Asn Ser Met Val Thr Glu	688
TAC GTG GAG CAC GGA CCC CTG GAT GTG TGG CTG CGG AGG GAG CGG GGC	2418
Tyr Val Glu His Gly Pro Leu Asp Val Trp Leu Arg Arg Glu Arg Gly	704
CAT GTG CCC ATG GCT TGG AAG ATG GTG GTG GCC CAG CAG CTG GCC AGC	2466
His Val Pro Met Ala Trp Lys Met Val Val Ala Gln Gln Leu Ala Ser	720
GCC CTC AGC TAC CTG GAG AAC AAG AAC CTG GTT CAT GGT AAT GTG TGT	2514
Ala Leu Ser Tyr Leu Glu Asn Lys Asn Leu Val His Gly Asn Val Cys	736
GGC CGG AAC ATC CTG CTG GCC CGG CTG GGG TTG GCA GAG GGC ACC AGC	2562
Gly Arg Asn Ile Leu Leu Ala Arg Leu Gly Leu Ala Glu Gly Thr Ser	752
CCC TTC ATC AAG CTG AGT GAT CCT GGC GTG GGC CTG GGC GCC CTC TCC	2610
Pro Phe Ile Lys Leu Ser Asp Pro Gly Val Gly Leu Gly Ala Leu Ser	768
AGG GAG GAG CCG GTG GAG AGG ATC CCC TGG CTG GCC CCC GAA TGC CTA	2658
Arg Glu Glu Arg Val Glu Arg Ile Pro Trp Leu Ala Pro Glu Cys Leu	784
CCA GGT GGG GCC AAC AGC CTA AGC ACC GCC ATG GAC AAG TGG GGG TTT	2706
Pro Gly Gly Ala Asn Ser Leu Ser Thr Ala Met Asp Lys Trp Gly Phe	800
GGC GCC ACC CTC CTG GAG ATC TGC TTT GAC GGA GAG GCC CCT CTG CAG	2754
Gly Ala Thr Leu Leu Glu Ile Cys Phe Asp Gly Glu Ala Pro Leu Gln	816
AGC CGC AGT CCC TCC GAG AAG GAG CAT TTC TAC CAG AGG CAG CAC CGG	2802
Ser Arg Ser Pro Ser Glu Lys Glu His Phe Tyr Gln Arg Gln His Arg	832
CTG CCC GAG CCC TCC TGC CCA CAG CTG GCC ACA CTC ACC AGC CAG TGT	2850
Leu Pro Glu Pro Ser Cys Pro Gln Leu Ala Thr Leu Thr Ser Gln Cys	848

- FIGURE 3B -

GAG CGT GTG CCC GTG TGC CAC CTG AGG CTG CTG GCC CAG GCC GAG GGG Glu Arg Val Pro Val Cys His Leu Arg Leu Leu Ala Gln Ala Glu Gly	1170 288
GAG CCC TGC TAC ATC CGG GAC AGT GGG GTG GCC CCT ACA GAC CCT GGC Glu Pro Cys Tyr Ile Arg Asp Ser Gly Val Ala Pro Thr Asp Pro Gly	1218 304
CCT GAG TCT GCT GCT GGG CCC CCA ACC CAC GAG GTG CTG GTG ACA GGC Pro Glu Ser Ala Ala Gly Pro Pro Thr His Glu Val Leu Val Thr Gly	1266 320
ACT GGT GGC ATC CAG TGG TGG CCA GTA GAG GAG GAG GTG AAC AAG GAG Thr Gly Gly Ile Gln Trp Trp Pro Val Glu Glu Glu Val Asn Lys Glu	1314 336
GAG GGT TCT AGT GGC AGC AGT GGC AGG AAC CCC CAA GCC AGC CTG TTT Glu Gly Ser Ser Gly Ser Ser Gly Arg Asn Pro Gln Ala Ser Leu Phe	1362 352
GGG AAG AAG GCC AAG GCT CAC AAG GCA TTC GGC CAG CCG GCA GAC AGG Gly Lys Lys Ala Lys Ala His Lys Ala Phe Gly Gln Pro Ala Asp Arg	1410 368
CCG CGG GAG CCA CTG TGG GCC TAC TTC TGT GAC TTC CGG GAC ATC ACC Pro Arg Glu Pro Leu Trp Ala Tyr Phe Cys Asp Phe Arg Asp Ile Thr	1458 384
CAC GTG GTG CTG AAA GAG CAC TGT GTC AGC ATC CAC CGG CAG GAC AAC His Val Val Leu Lys Glu His Cys Val Ser Ile His Arg Gln Asp Asn	1506 400
AAG TGC CTG GAG CTG AGC TTG CCT TCC CGG GCT GCG GCG CTG TCC TTC Lys Cys Leu Glu Leu Ser Leu Pro Ser Arg Ala Ala Ala Leu Ser Phe	1554 416
GTG TCG CTG GTG GAC GGC TAT TTC CGC CTG ACG GCC GAC TCC AGC CAC Val Ser Leu Val Asp Gly Tyr Phe Arg Leu Thr Ala Asp Ser Ser His	1602 432
TAC CTG TGC CAC GAG GTG GCT CCC CCA CGG CTG GTG ATG AGC ATC CGG Tyr Leu Cys His Glu Val Ala Pro Pro Arg Leu Val Met Ser Ile Arg	1650 448
GAT GGG ATC CAC GGA CCC CTG CTG GAG CCA TTT GTG CAG GCC AAG CTG Asp Gly Ile His Gly Pro Leu Leu Glu Pro Phe Val Gln Ala Lys Leu	1698 464
CGG CCC GAG GAC GGC CTG TAC CTC ATT CAC TGG AGC ACC AGC CAC CCC Arg Pro Glu Asp Gly Leu Tyr Leu Ile His Trp Ser Thr Ser His Pro	1746 480
TAC CGC CTG ATC CTC ACA GTG GCC CAG CGT AGC CAG GCA CCA GAC GGC Tyr Arg Leu Ile Leu Thr Val Ala Gln Arg Ser Gln Ala Pro Asp Gly	1794 496
ATG CAG AGC TTG CGG CTC CGA AAG TTC CCC ATT GAG CAG CAG GAC GGG Met Gln Ser Leu Arg Leu Arg Lys Phe Pro Ile Glu Gln Gln Asp Gly	1842 512
GCC TTC GTG CTG GAG GGC TGG GGC CGG TCC TTC CCC AGC GTT CGG GAA Ala Phe Val Leu Glu Gly Trp Gly Arg Ser Phe Pro Ser Val Arg Glu	1890 528
CIT GGG GCT GCC TTG CAG GGC TGC TTG CTG AGG GCC GGG GAT GAC TGC Leu Gly Ala Ala Leu Gln Gly Cys Leu Leu Arg Ala Gly Asp Asp Cys	1938 544
TTC TCT CTG CGT CGC TGT TGC CTG CCC CAA CCA GGA GAA ACC TCC AAT Phe Ser Leu Arg Arg Cys Cys Leu Pro Gln Pro Gly Glu Thr Ser Asn	1986 560

- FIGURE 3 c-

CTG ACC TAT GAG CCA ACC CAG AGG CCA TCA TTC CGC ACC ATC CTG CGT Leu Thr Tyr Glu Pro Thr Gln Arg Pro Ser Phe Arg Thr Ile Leu Arg	2898 864
GAC CTC ACC CGC GTG CAG CCC CAC AAT CTT GCT GAC GTC TTG ACT GTG Asp Leu Thr Arg Val Gln Pro His Asn Leu Ala Asp Val Leu Thr Val	2946 880
AAC CGG GAC TCA CCG GCC GTC GGA CCT ACT ACT TTC CAC AAG CGC TAT Asn Arg Asp Ser Pro Ala Val Gly Pro Thr Thr Phe His Lys Arg Tyr	2994 896
TTG AAA AAG ATC CGA GAT CTG GGC GAG GGT CAC TTC GGC AAG GTC AGC Leu Lys Lys Ile Arg Asp Leu Gly Glu Gly His Phe Gly Lys Val Ser	3042 912
TTG TAC TGC TAC GAT CCG ACC AAC GAC GGC ACT GGC GAG ATG GTG GCG Leu Tyr Cys Tyr Asp Pro Thr Asn Asp Gly Thr Gly Met Val Ala	3090 928
GTG AAA GCC CTC AAG GCA GAC TGC GGC CCC CAG CAC CGC TCG GGC TGG Val Lys Ala Leu Lys Ala Asp Cys Gly Pro Gln His Arg Ser Gly Trp	3138 944
AAG CAG GAG ATT GAC ATT CTG CGC ACG CTC TAC CAC GAG CAC ATC ATC Lys Gln Glu Ile Asp Ile Leu Arg Thr Leu Tyr His Glu His Ile Ile	3186 960
AAG TAC AAG GGC TGC TGC GAG GAC CAA GGC GAG AAG TCG CTG CAG CTG Lys Tyr Lys Gly Cys Cys Glu Asp Gln Gly Glu Lys Ser Leu Gln Leu	3234 976
GTC ATG GAG TAC GTG CCC CTG GGC AGC CTC CGA GAC TAC CTG CCC CGG Val Met Glu Tyr Val Pro Leu Gly Ser Leu Arg Asp Tyr Pro Arg	3282 992
CAC AGC ATC GGG CTG GCC CAG CTG CTG CTC TTC GCC CAG CAG ATC TGC His Ser Ile Gly Leu Ala Gln Leu Leu Leu Phe Ala Gln Gln Ile Cys	3330 1008
GAG GGC ATG GCC TAT CTG CAC GCG CAC GAC TAC ATC CAC CGA GAC CTA Glu Gly Met Ala Tyr Leu His Ala His Asp Tyr Ile His Arg Asp Leu	3378 1024
GCC GCG CGC AAC GTG CTG CTG GAC AAC GAC AGG CTG GTC AAG ATC GGG Ala Ala Arg Asn Val Leu Leu Asp Asn Asp Arg Leu Val Lys Ile Gly	3426 1040
GAC TTT GGC CTA GCC AAG GCC GTG CCC GAA GGC CAC GAG TAC TAC CGC Asp Phe Gly Leu Ala Lys Ala Val Pro Glu Gly His Glu Tyr Tyr Arg	3474 1056
GTG CGC GAG GAT GGG GAC AGC CCC GTG TTC TGG TAT GCC CCA GAG TGC Val Arg Glu Asp Gly Asp Ser Pro Val Phe Trp Tyr Ala Pro Glu Cys	3522 1072
CTG AAG GAG TAT AAG TTC TAC TAT GCG TCA GAT GTC TGG TCC TTC GGG Leu Lys Glu Tyr Lys Phe Tyr Tyr Ala Ser Asp Val Trp Ser Phe Gly	3570 1088
GTG ACC CTG TAT GAG CTG CTG ACG CAC TGT GAC TCC AGC CAG AGC CCC Val Thr Leu Tyr Glu Leu Leu Thr His Cys Asp Ser Ser Gln Ser Pro	3618 1104
CCC ACG AAA TTC CTT GAG CTC ATA GGC ATT GCT CAG GGT CAG ATG ACA Pro Thr Lys Phe Leu Glu Leu Ile Gly Ile Ala Gln Gly Gln Met Thr	3666 1120
GTT CTG AGA CTC ACT GAG TTG CTG GAA CGA GGG GAG AGG CTG CCA CGG Val Leu Arg Leu Thr Glu Leu Leu Glu Arg Gly Glu Arg Leu Pro Arg	3714 1136

- FIGURE 3D -

CCC GAC AAA TGT CCC TGT GAG GTC TAT CAT CTC ATG AAG AAC TGC TGG	3762
Pro Aep Lys Cys Pro Cys Glu Val Tyr His Leu Met Lys Aen Cys Trp	1152
GAG ACA GAG GCG TCC TTT CGC CCA ACC TTC GAG AAC CTC ATA CCC ATT	3810
Glu Thr Glu Ala Ser Phe Arg Pro Thr Phe Glu Aen Leu Ile Pro Ile	1168
CTG AAG ACA GTC CAT GAG AAG TAC CAA GGC CAG GCC CCT TCA GTG TTC	3858
Leu Lys Thr Val His Glu Lys Tyr Gln Gly Gln Ala Pro Ser Val Phe	1184
AGC GTG TGC	3867
Ser Val Cys	1187

6622100-1954563

Western blot analysis of Jak2 phosphorylation. The top panel shows a Western blot with molecular weight markers (215, 105, 70, 43 kDa) on the left. The lanes are labeled at the top: NRS, α Jak2, α Jak2 + Jak2 peptide, α Jak2 + Jak1 peptide. Each label has a '-' and a '+' sub-label. An arrow on the right points to the Jak2 band. The bottom panel is an autoradiography of the same blot, with an arrow pointing to the Jak2 band. The text "Probed with Anti-Jak2" is at the bottom.

- FIGURE 4 -

```

pileup.msf(Jak1) ..MQLYLNKE DGNAMAFCAK MRSFKKTEVK QVVP-ERQVE VTFVLLDRP
pileup.msf(Tyk2) MFLRHGMAR GSKFVG.... DGRQ PHAA-MGLK VLLHQAQPG
pileup.msf(Jak2) MGAACLTTE KEATSTSPVH QNGDIPGSAN SVQIEPVLQ VYLHSGQA
Consensus M-X--L-M-E -----A- -V---EPGL- V-LY-----

pileup.msf(Jak1) ....LRLGSG EYTAELCIR AAQSGSISPL CHNLFALYDE SKLWAPNR
pileup.msf(Tyk2) GEPWTFSES SLTAEEVCIH IAKVGIITP CFNLFALFDA QQVWLPNNH
pileup.msf(Jak2) EGEYLAFFSG EYVAEEICVA ASKAGGIPV YHNNFALMSE TERIVPPNH
Consensus -----L-FSG EYTAEE-CI- AA--GGITP- CHNLFAL-DE ---WYPPNH

pileup.msf(Jak1) IITVDKTSL RLHYRREYF TWHGCTDNE QSVTHSPKK QNGYEKRV
pileup.msf(Tyk2) ILIIPDASL MLYFRIRYF RWHOMPRE PAVTROPFG TEASD..QT
pileup.msf(Jak2) VFHIDSTRE DILYRIRYF PHWY..... CSQSS RYRYGVSRG
Consensus I--ID--TSL -L-YRIRYF -NWHG-N--S --V-RCSP-- ---Y--R-

pileup.msf(Jak1) PEATPLDAS SLEYLAQQQ YLINFIAPI RQPTSQDGH DIENECLMA
pileup.msf(Tyk2) AQOQLLDPA SFLEYLQGGK HEFVNDVASL WELSTEEIH HFNESCLMA
pileup.msf(Jak2) AEA-FLDDF VMSYLEAQR HDFVGHKV .....PVTH ETOECLMA
Consensus AEA-FLDD- S-EYLEAQQ- HDFV---A-- ----TE---H ---NECLMA

pileup.msf(Jak1) VLAISHAYM KXQQLPEPK DISKYIPE TLNKSIRQN LLTRMIRNV
pileup.msf(Tyk2) FLHCHLAIR HGIPLESAK KTSFKDCIPR SFRSHIRQHS ALTRLRINV
pileup.msf(Jak2) VLDMMRIAKE KDQTPAVIN SVSYKFLPK CVRAKIQDYH ILTRKEIYR
Consensus VL---H-A-- K---L-EV-K --SVK--IP- --R--IRQ-- -LTR-IRNV

pileup.msf(Jak1) FQDPIKEFVN KTCDSVST HDLKVYLAT LETLTHYGA EIFETSMILI
pileup.msf(Tyk2) FRRLRFQ. ....PRLSQ QWAVVYLAT LERLAPRGQ ERVPCHLRL
pileup.msf(Jak2) FRRLIQF.. ...SQCKATA RLNLXVLIN LETLQSAYT EQEV.....
Consensus FRRL--F-- -----S- --LAVYLAT LETL---FGT E-FEV--L--

```

- FIGURE 5A -

pileup.msf(Jak1)	SSENELRGH	SNDS.....KNTLK	RKLEINVKH	KDDERNKLE	EWNFSYFFE	QIQWRQKPN
pileup.msf(TyK2)	LAQNEEPCY	IRDSGVAPTD	SCRFQASLF	GKAKAHAKF	QCAPADREP	LMAYFCDFP	QIQWNEEVE
pileup.msf(Jak2)E-----C-	-----E-----	-----KE	-----K-K	-----G	-----G	QIQWS....
Consensus							QIQWS....
pileup.msf(Jak1)	VPVKE....KNTLK	SCRFQASLF	GKAKAHAKF	QCAPADREP	LMAYFCDFP	QIQWNEEVE
pileup.msf(TyK2)E-----C-	-----E-----	-----KE	-----K-K	-----G	-----G	QIQWS....
pileup.msf(Jak2)E-----C-	-----E-----	-----KE	-----K-K	-----G	-----G	QIQWS....
Consensus							QIQWS....
pileup.msf(Jak1)	ITHIVKE..SVV	SINKQNKNM	ELKLSRREA	LSFVSLVDGY	LSFVSLVDGY	LSFVSLVDGY
pileup.msf(TyK2)	ITHVVKSE..HCV	SIHQNKQLK	ELSLSPRAA	LSFVSLVDGY	LSFVSLVDGY	LSFVSLVDGY
pileup.msf(Jak2)	IDIVSIQAN	QECSENRIV	TVHKQDNVL	EIELSLKEA	LSFVSLVDGY	LSFVSLVDGY	LSFVSLVDGY
Consensus	ITHVVKSE..V	SIHQNK-L	EL-LSSR-EA	LSFVSLVDGY	LSFVSLVDGY	LSFVSLVDGY
pileup.msf(Jak1)	FLRTADAHY	LCTDVAPPLI	VHNIDGCHG	PICTEYAIK	LQEGSEEGM	LR....PEDGL	LR....PEDGL
pileup.msf(TyK2)	FLRTADSSHY	LCEHVAPPL	VNSTDQCHG	PISMDFFQAK	LR....PEDGL	LR....PEDGL	LR....PEDGL
pileup.msf(Jak2)	FLRTADAHY	LCEHVAPPAV	LENHSHCHG	PISMDFFQAK	LR....PEDGL	LR....PEDGL	LR....PEDGL
Consensus	FLRTADAHY	LC-EVAP--	V-NI---CCHG	PI---FAL-L	LR--G-E-GL	LR--G-E-GL	LR--G-E-GL
pileup.msf(Jak1)	YVLRNSCTDF	LLMLNTVTOG	QKSAQDGOK	QNFQFIE	VQNFYSLHG	VQNFYSLHG	VQNFYSLHG
pileup.msf(TyK2)	YVLRNSCTDF	YLLMTVA..	QKSAQDGOK	QNFQFIE	VQNFYSLHG	VQNFYSLHG	VQNFYSLHG
pileup.msf(Jak2)	YVLRNSCTDF	YLLMTVA..	QKSAQDGOK	QNFQFIE	VQNFYSLHG	VQNFYSLHG	VQNFYSLHG
Consensus	YVLRNS-DF	YLLMTVA..	QKSAQDGOK	QNFQFIE	VQNFYSLHG	VQNFYSLHG	VQNFYSLHG
pileup.msf(Jak1)	WDRFSPSYRE	LMNLAKQIL	RTDNISFVLK	RCOCXPKEI	SNLIV....	SNLIV....	SNLIV....
pileup.msf(TyK2)	WDRFSPSYRE	LMNLAKQIL	RTDNISFVLK	RCOCXPKEI	SNLIV....	SNLIV....	SNLIV....
pileup.msf(Jak2)	WDRFSPSYRE	LMNLAKQIL	RTDNISFVLK	RCOCXPKEI	SNLIV....	SNLIV....	SNLIV....
Consensus	WDRFSPSYRE	LMNLAKQIL	RTDNISFVLK	RCOCXPKEI	SNLIV....	SNLIV....	SNLIV....
pileup.msf(Jak1)	..ATKQAEW	QPVYSUQLS	FDRLKNDII	QSHLGRGTR	THYLSGTL..	THYLSGTL..	THYLSGTL..
pileup.msf(TyK2)	..ATKQAEW	QPVYSUQLS	FDRLKNDII	QSHLGRGTR	THYLSGTL..	THYLSGTL..	THYLSGTL..
pileup.msf(Jak2)	..ATKQAEW	QPVYSUQLS	FDRLKNDII	QSHLGRGTR	THYLSGTL..	THYLSGTL..	THYLSGTL..
Consensus	..ATKQAEW	QPVYSUQLS	FDRLKNDII	QSHLGRGTR	THYLSGTL..	THYLSGTL..	THYLSGTL..

- FIGURE 5B -

pileup.msf(Jak1)D	YDEEGTAE	K....KIKVI	LKVLPDSHRD	ISLAFFEAS
pileup.msf(Tyk2)	EGSGDPBEGK	MDDEDVPRG	RDRGQLRVV	LKVLPDSHRD	IACAFETAS
pileup.msf(Jak2)VGD	YQQLKTEVL	LKVLDRAHRN	YSSSFEFAS
Consensus	-----	--DE----	-----V--	-----K--V-	ISLAFFEAS
pileup.msf(Jak1)	KMRQVSHKHI	VYLXGVCVRD	VENIMVEEFV	EGGFLDLPWH	RKSDALTPW
pileup.msf(Tyk2)	KMSQVSHTHL	AFVHGVCVRG	PENIMTTEVY	EHGFLDVLWR	REHGHPWAW
pileup.msf(Jak2)	KMSQLSHKHL	VLANGVCVCG	ENILVQEFV	KFGSLDTYLK	KNKNSINILW
Consensus	KMSQVSHKHL	V--YGVCVRG	-ENIMV-EFV	E-GPLD--L-	R-----W
pileup.msf(Jak1)	KFVVAQGLAS	ALSYLEDKDL	VHGVCCTKNL	LLAR.EGIDS	DIGPFILSD
pileup.msf(Tyk2)	KAVVAQGLAS	ALSYLENKUL	VHGVCGRNI	LLAR.LGLAE	GNPFILSD
pileup.msf(Jak2)	KLGVAQQLAW	AMHFLKESKL	IHGRCVAKNI	ILIREEDRT	GNPFILSD
Consensus	K--VAQGLAS	ALSYL-L-L	VHGVC-XNI	LLAR-EG---	G--PFILSD
pileup.msf(Jak1)	PGIFVSVLIR	QECIERIPWI	APCEVDSKN	.LSVADKMS	FOTLMEICY
pileup.msf(Tyk2)	PGVGLGALSR	EEVERIPWL	APECLPGAN	SLSTANDKMG	FGATLEICF
pileup.msf(Jak2)	PGISITVLPK	DILQERIPWV	PECIENPKN	.LNLATDKMS	FOTLMEICS
Consensus	PGI---VL-R	-E--ERIPW-	APEC-E-KN	-LS-A-DKMS	FOTLMEIC-
pileup.msf(Jak1)	NGEIPDKDXT	LIEKREYES	RCRPVTPSCK	ELADLMTCH	NYDPNORFF
pileup.msf(Tyk2)	DGEAPLOQRS	PSEKHYQR	QHRLEPSCP	QLATLSOCL	TYEPTORPS
pileup.msf(Jak2)	GDKPLSALD	SQKLQFYED	KHQLPAFKWT	ELANLINCH	DYEPDFRAF
Consensus	-GE-PL----	--EKS-FYE-	-HRLP-PSC-	ELA-L--CH	-YEP-QRP-F
pileup.msf(Jak1)	RAIMRDINKLE	EQN.PDI....	.VSEKOPTIE	VDFTEKRR
pileup.msf(Tyk2)	RTILRDITRLQ	PHLADV...	.LTVPNPSPA	SDPTVFKRY
pileup.msf(Jak2)	RAVIDRLNSL	FTPDYELLTE	NDMLPNRIG	ALGFGAFED	RDPTQFERH
Consensus	RAI-RDLN-L	-----E	--NLPD----	-L-----	-DPT-FEKR-
pileup.msf(Jak1)	LKKIRDLGEG	HFGKVELCRY	DPECNMGEG	VAVKSLPES	GGNHIALKK
pileup.msf(Tyk2)	LKKIRDLGEG	HFGKVELCRY	DPTNDGTGM	VAVKALKADC	CPHRRSGWKQ
pileup.msf(Jak2)	LKFQQLGEG	NFGSVEMCRY	DPLQDNTGEV	VAVKLQ.HS	TEEHLRDER
Consensus	LK-IRDLGEG	HFGKVELCRY	DP--DNTGE-	VAVK-LK--S	G--H-D-K-
pileup.msf(Jak1)	EIEILRLYH	ENIVKYGIC	MEDGGNGIKL	IMEFPGSL	KEYLPKNKK
pileup.msf(Tyk2)	EIEILRLYH	EHIKYKGC	EDQGEKSLQ	VMEYVLGSL	ROYLP..RHS
pileup.msf(Jak2)	EIEILSLQH	DNVYKVCQ	YSAGRNRL	IMEIYFGL	RDYLQKHKR
Consensus	EIEIL-LYH	ENIVKYG-C	--G---L-L	IMEYLP-GSL	RDYLPK-K--

1. The first step is to identify the problem. In this case, the problem is that the system is not working properly.

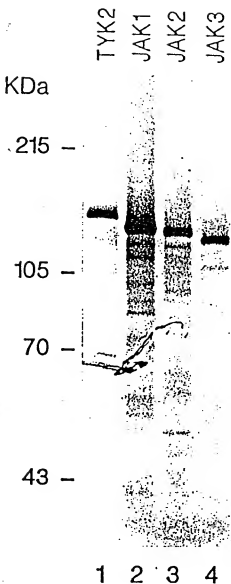


FIGURE 7A

KDa

215 -

105 -

70 -

43 -

1 2 3 4

FIGURE 7B

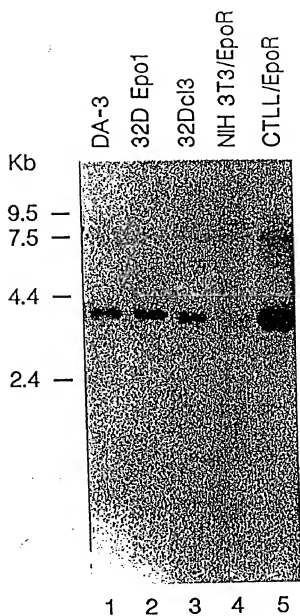


FIGURE 8

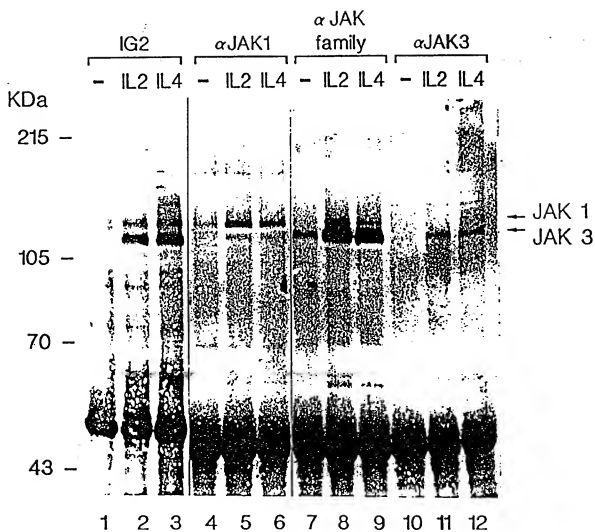


FIGURE 9A

Western blot analysis of JAK3 phosphorylation. The blot shows three lanes: lane 1 (control, -), lane 2 (IL2), and lane 3 (IL4). Molecular weight markers are indicated on the left at 215, 105, and 70 kDa. An arrow on the right points to the JAK3 band at approximately 105 kDa. Phosphorylation of JAK3 is observed in lanes 2 and 3 compared to lane 1.

20

0037967-091200

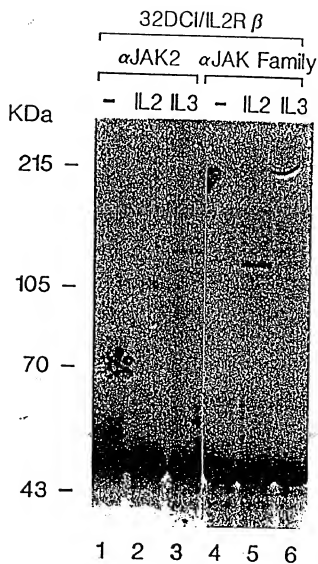


FIGURE 9C

00397967 004799
661150 19615560

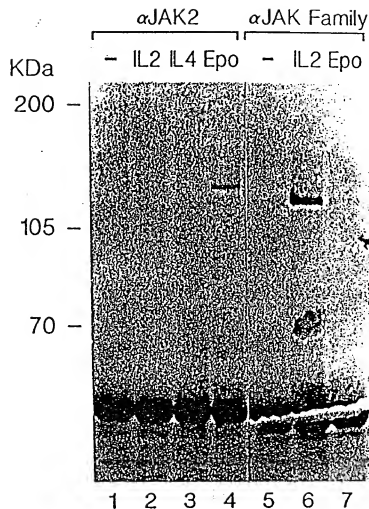


FIGURE 9D

Cotxf:
 gp130F - + + + + + + + +
 Jak1 - - - + + - - + +
 Jak2 - - - - - + + + +

 IL6 + sIL6R: + - + - + - + - +

gp130 →

1 2 3 4 5 6 7 8 9

FIGURE 10

Transfect :
Cotransfect:

Jak1

Jak2

LIFR

LIFRT74



FIGURE 11

09397967 "001722

PHOSPHOTYROSINE IMMUNOBLOT IN VITRO KINASE ASSAY

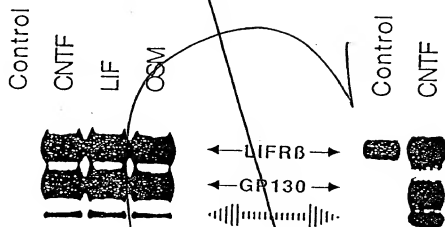
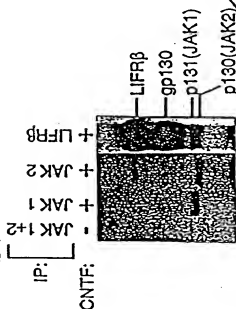


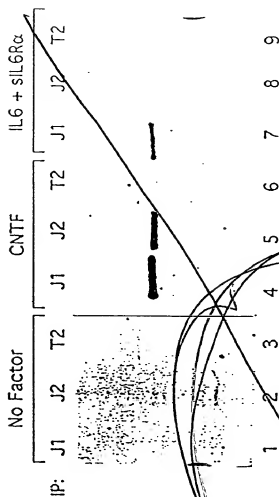
FIGURE 12

662760 29616663

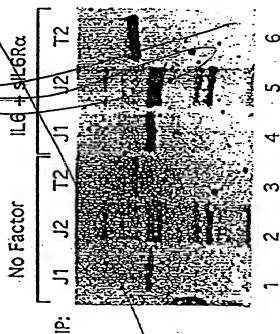
A. EW-1 Cells



B. EW-1 Cells



C. U266 Cells



D. SK-MES Cells

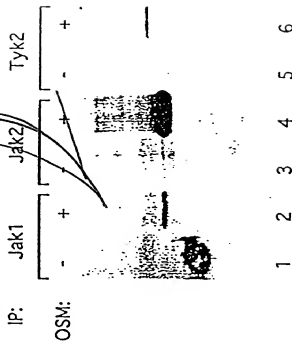


FIGURE 13 A-D